SYSTEMATIC REVIEW

Etiology of Pregnancy-related Acute Kidney Injury among Obstetric Patients in India: A Systematic Review

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Abstract

Background: Pregnancy-related acute kidney injury (PRAKI) is an important cause of fetomaternal mortality and morbidity in developing countries. We undertook a systematic review to identify the causes of PRAKI among obstetric patients in India.

Materials and methods: We systematically searched PubMed, MEDLINE, Embase, and Google Scholar using appropriate search terminology between 1 January 2010 to 31 December 2021. Studies reporting the etiology of PRAKI among obstetric patients (pregnant and within 42 days postpartum) in India were included for evaluation. Studies done in any other geographical location besides India were excluded. We also excluded studies done in any one trimester or any specific subgroup of patients [e.g., postpartum acute kidney injury (AKI), postabortal AKI]. A five-point questionnaire was used to assess the risk of bias in included studies. The results were synthesized as per preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.

Results: A total number of 7 studies with 477 participants were included for analysis. All were single-center descriptive observational studies either done in tertiary care public or private hospitals. Sepsis (mean, 41.9%; median, 49.4%; and range, 6–56.1%) was the most common cause of PRAKI followed by hemorrhage (mean, 22.1%; median, 23.5%; and range, 8.3–38.5%) and pregnancy-induced hypertension (mean, 20.9%; median, 20.7; and range, 11.5–39%). Among these seven studies, five were of moderate quality, one was of high quality, and another one was of low quality. Our study is limited due to the lack of consensus definition of PRAKI in literature and heterogeneity in reporting methods. Our study highlights the need for a structured reporting format for PRAKI to understand the true disease burden and take control measures.

Conclusion: There is a moderate quality of evidence to suggest that sepsis followed by hemorrhage and pregnancy-induced hypertension are the commonest causes of PRAKI in India.

Keywords: Maternal mortality, Pregnancy-induced hypertension, Pregnancy-related acute kidney injury, Sepsis.

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Highlights

- Pregnancy-related acute kidney injury is associated with significant feto–maternal morbidity and mortality.
- There is limited literature in this field due to lack of consensus definition and heterogeneous data.
- Our study found that sepsis followed by hemorrhage and pregnancy-induced hypertension are the commonest causes of PRAKI in India.
- Among the patients with PRAKI undergoing renal biopsy for non-recovery of renal function, acute cortical necrosis (ACN) was the most common cause, followed by acute tubular necrosis (ATN).
- We propose a standard reporting format for PRAKI to generate comparable data and guide policymakers.

Introduction

The epidemiology of PRAKI varies globally, with developing countries bearing the burden of PRAKI caused by sepsis and hemorrhage. In contrast, the developed countries experience a larger share of PRAKI caused by chronic illnesses like hypertension, diabetes, obesity, autoimmune disorders, etc.[1,2] Irrespective of the cause, kidney injury in pregnancy is associated with an increased feto–maternal mortality and morbidity. Although, with the legalization of abortion in many countries, the rate of postabortal sepsis and related AKI has significantly declined, PRAKI remains an area of concern in middle- and low-income countries.[2]

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By and large, the causes of PRAKI can be classified into three categories as follows; diseases specific to pregnancy [e.g., pre-eclampsia/hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome], diseases incidental to pregnancy (e.g., dengue and malaria), and diseases aggravated by pregnancy (e.g., lupus nephritis). Other methods of classifying PRAKI include the site of

origin of the disease process (prerenal, renal, and postrenal causes) or timing of PRAKI (first trimester, second trimester, third trimester, and postpartum causes).[3,4]

The true incidence of PRAKI remains unknown. This is because pregnancy per se is associated with a 50% increase in glomerular filtration rate leading to a 50% drop in serum creatinine values from the pre-pregnant states.[5] As a result, if the absolute value of serum creatinine is used for diagnosing AKI in pregnancy, many patients in the early stages of kidney injury will be missed. On the other hand, using a rise in serum creatinine from baseline value requires knowledge of baseline serum creatinine for a given patient, which is seldom available. Different definitions of AKI in pregnancy have been used in literature, ranging from drop-in urine output to a rise in serum creatinine or the need for dialysis. The "Kidney Disease: Improving Global Outcomes (KDIGO)" definition is the standard of AKI definition worldwide, but its validation in pregnant patients is an area of research.[6]

The variation in the classification of causes of PRAKI and the use of different definitions have made the reporting heterogeneous and difficult to compare. Understanding the true burden of PRAKI is important for appropriate resource allocation and timely transfer of sick patients to dialysis-equipped centers by primary and community health care centers across the country.[7] The systematic review is a popular method to summarize medical literature related to a particular field. We conducted this systematic review with the following objectives:

- Primary objective: To identify the causes of PRAKI among obstetric patients in India
- Secondary objectives
  - To estimate the incidence rate of PRAKI among obstetric patients in India.
  - To determine the maternal and renal outcome of PRAKI among obstetric patients in India.

Materials and Methods

Criteria for Including Studies

Population

Observational studies reporting causes of PRAKI among obstetric patients in India were considered eligible for qualitative analysis; PRAKI was defined as AKI occurring during pregnancy or within 42 days following delivery. We excluded the studies done in any other geographical location besides India. Studies that reported causes of AKI in only postpartum patients or anyone trimester were also excluded.

Definition of PRAKI

To be included in the systematic review, the study had to use an appropriate AKI definition. Also, AKI was defined as per KDIGO definition (increase in serum creatinine above 0.3 mg/dL from baseline or above 1.5 times from the reference value or drop in urine output below 0.5 mL/kg/hour for 6–12 hours). Studies using risk, injury, failure, loss, end-stage (RIFLE) criteria or oliguria/anuria (urine output below 400 mL/day) with azotemia (serum creatinine above 2 mg/dL) as criteria for defining AKI were also included as some of the studies were done before KDIGO definition came into routine clinical use.

Etiology of PRAKI

To be included for analysis, the study had to report causes of PRAKI in the study population in an explicit manner. We excluded studies that did not report the etiology of PRAKI appropriately or reported more than one cause for PRAKI in most patients. Studies using duplicate data with the same information for more than one publication were also excluded.

Criteria for Assessing Renal Outcome of PRAKI

To be included for outcome analysis, the study had to report renal outcome of PRAKI under following headings: (1) Those showing complete renal recovery on follow-up at 3 months (normal serum creatinine with normal urine output. (2) Those showing progression to chronic kidney disease (with or without need for dialysis). Chronic kidney disease was defined as per KDIGO definition, which includes structural or functional damage to the kidney which lasts for more than three months. This requires fulfilling either of the following criteria for more the 3 months, that is, fall in glomerular filtration rate (GFR) below 60 mL/minutes/1.73 m^2 or presence of markers of kidney damage (albuminuria above 30 mg/day, structural abnormality of kidney on imaging or histology, abnormalities in urinary sediments like hematuria, red cell casts, etc.).[8]

Incidence Rate

Incidence rate of PRAKI was defined as the number of cases of PRAKI divided by the number of deliveries during the study duration multiplied by 10^n.

Literature Search

An electronic data search was done in PubMed, Medline, Embase, and Google Scholar using search terminology "pregnancy-related acute kidney injury," "obstetric acute kidney injury," "pregnancy and acute kidney injury," "pregnancy and acute renal insufficiency," and "pregnancy-related acute renal insufficiency" by two authors (AA and MG) independently. All observational studies between 1 January 2010 to 31 December 2021 were included. References of the relevant articles were also searched manually, and relevant studies were included for analysis. Two authors (AA and MG) independently searched the records for eligibility using the study selection criteria described above. Any difference of opinion was discussed with the third author (AA) and resolved with mutual consensus.

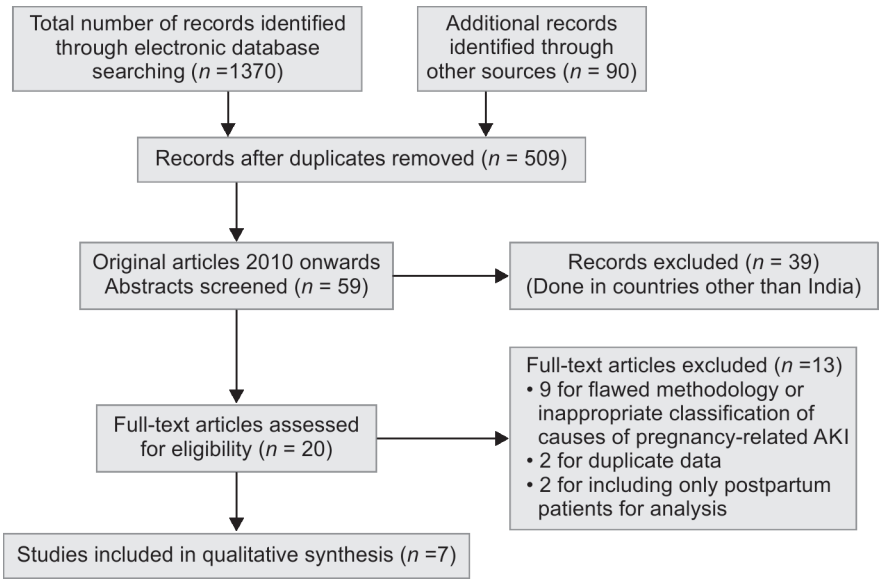
Data Extraction

Data extraction was done using a data extraction form under the following headings: Study title, first author, aims and objectives, study design, number of centers, place, year, and duration of the study. We collected information regarding demographic characteristics of the study cohort, causes of PRAKI, number of hemodialysis sessions given, duration of follow-up, indications for renal biopsy, and renal and maternal outcomes. The data were then entered into excel sheets and double-checked for accuracy.

Study Quality Assessment

Quality assessment for epidemiological studies can be done by using a standard assessment tool or designing a customized questionnaire specifically for the review. Among the standard assessment tools, Joanna Briggs Institute (JBI) critical appraisal checklist can be used for studies reporting prevalence data.[9] As all studies qualifying for analysis were descriptive observational cohort studies, we preferred to customize our own tool. We took guidance from a systematic review done by WHO on causes of maternal mortality and the JBI critical appraisal checklist.[9,10] We designed our own 5-point questionnaire to assess the methodological quality of the studies in terms of the following attributes: (1) Appropriately defined inclusion and exclusion

Flowchart 1: PRISMA flowchart



criteria; (2) The cause of PRAKI is clearly defined and confirmed *via* clinical, laboratory, imaging and/or biopsy findings; (3) All common causes of PRAKI included in the classification; (4) Less than 10% patients having unclassified causes of PRAKI; (5) Renal outcome, as well as maternal outcome, is reported appropriately. We did not include fetal outcomes in our quality assessment questionnaire tool because most of the studies were done in nephrology departments and fetal outcomes were not available. A scoring system was used to grade the quality of evidence, with each question carrying 1 point. Studies that answered all five questions appropriately were given 5 points and graded as high quality. Studies with a score between 3 and 4 were graded as moderate-quality evidence, while studies with a score of less than three were graded as low-quality evidence. Studies with a score of less than two were graded as very low-quality evidence and were excluded from the study.

Statistical Analysis

Categorical variables are represented as frequencies and percentages. Data regarding the causes of PRAKI, and maternal and renal outcomes, were extracted from individual studies and presented in mean, median, and range of the values. Prism, v.5.0 (Carlsbad, California, USA) and MedCalc software were used for statistical analysis.

Results

Our study results showed 1,370 records *via* electronic search. Another 90 records were identified *via* a manual search of the bibliography of relevant articles. After removing the duplicates, reviews, case reports, and studies done outside India, the full text of 20 articles was retrieved. Thirteen studies were excluded due to methodological issues (Flowchart 1).[11–23] A total of 7 studies, including 477 participants, qualified for final analysis.[24–30] These studies enrolled participants from obstetrics or nephrology departments. Five studies were of moderate quality evidence (score: 3–4) while one study was high quality (score: 5), and one study was low quality (score: 2) (Table 1).

Study Characteristics (Table 2)

There were two studies from North India (Lucknow and Patna); two from South India (Chennai and Madurai); and one each from central (Indore), western (Ahmedabad), and eastern India (Kolkata).[24–30] All were single-center prospective observational (descriptive) studies except for one study from Lucknow, Uttar Pradesh, India, a retrospective observational (descriptive) study. Four studies were conducted in the nephrology department, while three were conducted in collaboration with the obstetrics and gynecology department and the nephrology department.[24–30] The total number of patients in each study ranged from 18 to 130. All studies were conducted in government hospitals except for one study from Ahmedabad, Gujarat, India, which was conducted in a private tertiary care center.[28] All studies reported third trimester/postpartum as the most common phase of presentation of PRAKI. The study from Lucknow included only those patients who underwent dialysis.[29] Three studies used the KDIGO definition of AKI, one study used the need for dialysis, and three used oligoanuria/rise in serum creatinine as defining criteria for AKI.[24–30]

Causes of PRAKI

Sepsis was the most common cause of PRAKI in most of the studies (mean, 41.9%; median, 49.4%; and range 6–56.1%). Other causes included hemorrhage (mean, 22.1%; median, 23.5%; and range, 8.3–38.5%), pregnancy-induced hypertension (mean, 20.9%; median, 20.7; and range, 11.5–39%) and thrombotic microangiopathies (TMAs) (mean, 4.7%; median, 2.0%; and range, 2–17.3%). There were miscellaneous/undiagnosed cases like tropical fever, acute fatty liver of pregnancy, etc., in less than 10% of cases (mean, 7.1%; median, 4.9%; and range, 0–22%) (Table 3).

Renal Biopsy Findings

Five studies reported renal biopsy findings.[25,27–30] Three studies used nonrecovery of renal function at 3 weeks as the indication for renal biopsy, while two studies used 4–6 weeks as the cut-off for renal biopsy. Acute cortical necrosis (mean, 48.3%; median, 50.0%; range, 17–80%) was the most common cause of non-recovery

Table 1: Study quality assessment

S.No.	Author and year of publication	Appropriate eligibility and inclusion criteria clearly defined	Cause of AKI clearly defined confirmed via clinical findings, laboratory testing and biopsy when needed	All common causes (sepsis, hemorrhage, pregnancy-induced hypertension, TMAs) of PRAKI included	Unclassified causes of PRAKI <10%	Renal and maternal outcome given including causes leading to death	Total score
1	Gayathiri et al. (2020)	N	N	N	Y	Y**	2
2	Saini et al. (2020)	N	Y	Y	Y	Y**	4
3	Malviya et al. (2020)	Y	N	Y	Y	N*	3
4	Parween et al. (2018)	Y	Y	N	Y	N*	3
5	Vineet et al. (2016)	Y	Y	Y	Y	Y**	5
6	Krishna et al. (2015)	Y	Y	Y	Y	N*	4
7	Gopalakrishnan et al. 2015	N	Y	Y	Y	Y**	4

Y, yes; N, no; PRAKI, pregnancy-related acute kidney injury

of renal failure followed by ATN mean, 20.4%; median, 20%; and range 0–37.5%). Other causes include TMAs (mean, 20.9%; median, 20.7%; and range, 11.5–39%) and glomerular diseases (mean, 20.9%; median, 20.7%; and range 11.5–39%) (Table 4).

Renal Outcome

At 3 months follow-up, more than 50% patients showed complete renal recovery in all but one study (mean, 56.5%; median, 55.9%; and range, 33.3–80%) (Fig. 1). Less than one-fifth of the patients progressed to chronic kidney disease with or without dialysis need (mean, 17.5%; median, 14.4%; range, 6–36.2%). There were 13.5% of patients who were lost to follow-up in two studies and 3.8% in one study. Other studies had not lost to follow-up.

Maternal Mortality

Maternal mortality ranged from 7.7% to 33.3% (mean, 20.8%; median, 19%). There is heterogeneity in reporting of maternal mortality among the studies. The study done by Vineet et al. has reported 14 (26.92%) deaths at the time of discharge and another 3 (5.77%) deaths at 3 months follow-up, thus leading to total 17 (32.7%) deaths.[28] The study by Saini et al. has reported 20 (25%) deaths at 28 days.[25] Other studies have not clearly mentioned whether death occurred during hospital stay or follow-up period. Table 2 mentions the total number of deaths and their percentage in different studies.

Cause of Maternal Mortality

Among the five studies reporting maternal mortality, sepsis was the most common cause in all except one study (mean, 56.4%; median, 58.8%; and range, 16–80%)[24,25,28–30] (Fig. 2). Other causes being pregnancy induced hypertension (mean, 16%; median, 16%; and range 5.5–23.5%), and hemorrhage (mean, 12.1%; median, 10%; and range, 0–33%), respectively.

Discussion

The relationship between pregnancy and AKI is unique and important due to the high predisposition for feto–maternal mortality and morbidity, difficulty in early diagnosis, and progression to chronic kidney disease in a subset of the population. Mostly, AKI occurs in pregnancy as a complication of another pregnancy-related condition like pre-eclampsia, hemorrhage, and postabortal or postpartum sepsis. Therefore, appropriate, and timely management of these conditions can help reduce the incidence and subsequent morbidity due to PRAKI. The current systematic review evaluates the causes of AKI in 477 patients with PRAKI from 7 studies done in India.

Our study shows sepsis as the most common cause of PRAKI in India, accounting for around 40 to 50% of the cases. We found postpartum sepsis as the leading cause of sepsis among the patients with PRAKI. Postpartum sepsis occurs following breach in asepsis during normal vaginal delivery or during cesarean section. Most studies included in the current systematic review have not mentioned whether postpartum sepsis occurred following normal delivery or cesarean section. Two studies from North India (one from Lucknow and one from Patna) reported a high rate of postabortal sepsis, which accounted for around one-fourth of PRAKI cases.[27,29] This highlights the regional inequity in healthcare facilities, awareness, and social status of women in some parts. These findings also echo with high MMR in some states in India (Uttar Pradesh, 197; Bihar, 149; Madhya Pradesh, 173 – per 1,00,000 live births) as compared to other parts of the country (Kerala, 43; Tamil Nadu, 60; Andhra Pradesh, 65 – per 1,00,000 live births).[31,32]

Besides postpartum and postabortal sepsis, four studies have reported other causes of sepsis like intrauterine death, pyelonephritis, and urinary tract infection.[26–29]

Among the other causes of PRAKI, TMAs require special mention because timely intervention with plasmapheresis and specific therapy (eculizumab for complement mediated hemolytic uremic syndrome) can bring favorable outcome in selected patients. Four studies reported TMAs in our systematic review, with maximum number of cases coming from prospective study by Saini et al. done in a government teaching hospital in Kolkata, West Bengal, India.[25,26,29,30] Frequently, the diagnosis of TMA is delayed in resource limited settings leading to high mortality and morbidity. However, maintaining a high index of suspicion in patients with

Table 2: Study characteristics; PRAKI in India (2010 onward)

S.No.	Author and year of publication	Study design	Inclusion criteria for AKI	Government/ private hospital	Location	Study period (years)	Department where the study was conducted	Total cases	Patients underwent HD	Age (mean ± SD)	Trimester at the time of presentation of AKI			Maternal mortality: Total Number of deaths
											First post-partum (%)	Second post-partum (%)	Third post-partum (%)	
1	Gayathiri et al. (2020)	Pros*	KDIGO	G**	Madurai	1	OBG and nephrology	18	6 (33%)	27 ± 4.2	6	11	83	6 (33%)
2	Saini et al. (2020)	Pros*	KDIGO	G**	Kolkata	2	OBG and nephrology	81	68 (84%)	23.6 ± 4.6	4.9	6.2	88.9	20 (25%)
3	Malviya et al. (2020)	Pros*	KDIGO	G**	Indore	1.5	Nephrology	60	8 (13.3%)	29.0 ± 6.3	NA	NA	NA	8 (13.3%)
4	Parween et al. (2018)	Pros*	Oliguria/anuria with azotemia (serum creatinine >2 mg%)	G**	Patna	1	OBG and Nephrology	38	30 (79%)	27	16	21	63	5 (13.2%)
5	Vineet et al. (2016)	Pros*	Oliguria/anuria with azotemia (serum creatinine >2 mg%)	P##	Ahmedabad	1.5	Nephrology	52	44 (84.6%)	26.2	NA	NA	NA	17 (32.7%)
6	Krishna et al. (2015)	Retro#	PRAKI requiring dialysis	G**	Lucknow	6	Nephrology	98	98 (100%)	28.8 ± 5.1	15.3	28.6	56.2	18 (18.4%)
7	Gopalakrishnan et al. (2015)	Pros*	Serum creatinine >1.5 times or oliguria	G**	Chennai	5	Nephrology	130	96 (74%)	25.4 ± 4.7	4	9	87	10 (8%)

*Prospective; **Government; #Retrospective, ##Private; AKI, acute kidney injury; HD, hemodialysis; KDIGO, kidney disease improving global outcomes; NA, not available; OBG; obstetrics and gynaecology; PRAKI, pregnancy-related acute kidney injury

Table 3: Causes of PRAKI in India (2010 onward)

		Sepsis								
S.No.	*Author and year of publication*	*Postabortal*	*Postpartum*	*Others*	*Total*	*Hemorrhage*	*Pregnancy-induced hypertension*	*TMAs*	*Hypovolemia*	*Others*
1	Gayathiri et al. (2020)	NA	NA	NA	01 (6%)	06 (33%)	07 (39%)	0	0	14 (22%)
2	Saini et al. (2020)	NA	NA	NA	40 (49.4%)	13 (16%)	10 (12.3%)	14 (17.3%)	0	4 (4.9%)
3	Malviya et al. (2020)	2 (3.3%)	19 (31.7%)	9 (15%)	30 (50%)	5 (8.3%)	14 (23.3%)	3 (5%)	7 (11.6%)	1 (1.6%)
4	Parween et al. (2018)	9 (23.6%)	10 (26.3%)	1 (2.6%)	20 (52.6%)	9 (23.6%)	8 (21%)	0	0	1 (2.6%)
5	Vineet et al. (2016)	3 (5.7%)	8 (15.3%)	10 (9.2%)	21 (40.4%)	20 (38.5%)	6 (11.5%)	0	0	5 (9.6%)
6	Krishna et al. (2015)	25 (25.5%)	23 (23.5%)	7 (7.1%)	55 (56.1%)	23 (23.5%)	18 (18.4%)	2 (2%)	0	0
7	Gopalakrishnan et al. (2015)	4 (3%)	47 (36.1%)	0	51 (39.1%)	16 (12.3%)	27 (20.7%)	11 (8.4%)	13 (10%)	12 (9.2%)

NA, not available

Table 4: Renal biopsy findings in studies done on PRAKI in India (2010 onward)

S.No.	Author and year of publication	Total number of biopsies done	ACN	ATN	TMAs	Glomerular disease	Others	Threshold for doing biopsy
1	Gayathiri et al. (2020)	NA	NA	NA	NA	NA	NA	Persistent renal failure for above 3 weeks
2	Saini et al. (2020)	24	4 (17%)	6 (25%)	13 (54%)	1 (4%)	0	Non-recovery of renal function above 3 weeks
3	Malviya et al. (2020)	NA	NA	NA	NA	NA	NA	NA
4	Parween et al. (2018)	5	3 (60%)	0	0	0	2 (40%)	Oliguric/dialysis required at 4–6 weeks
5	Vineet et al. (2016)	10	8 (80%)	2 (20%)	0	0	0	Dialysis required for above 3 weeks
6	Krishna et al. (2015)	16	8 (50%)	6 (37.5%)	2 (12.5%)	0	0	Non-recovery of renal function for above 4 weeks
7	Gopalakrishnan et al. (2015)	46	16 (34.7%)	9 (19.5%)	11 (23.9%)	9 (19.5%)	1 (2.1%)	Persistent renal failure for above 3 weeks

NA, not available

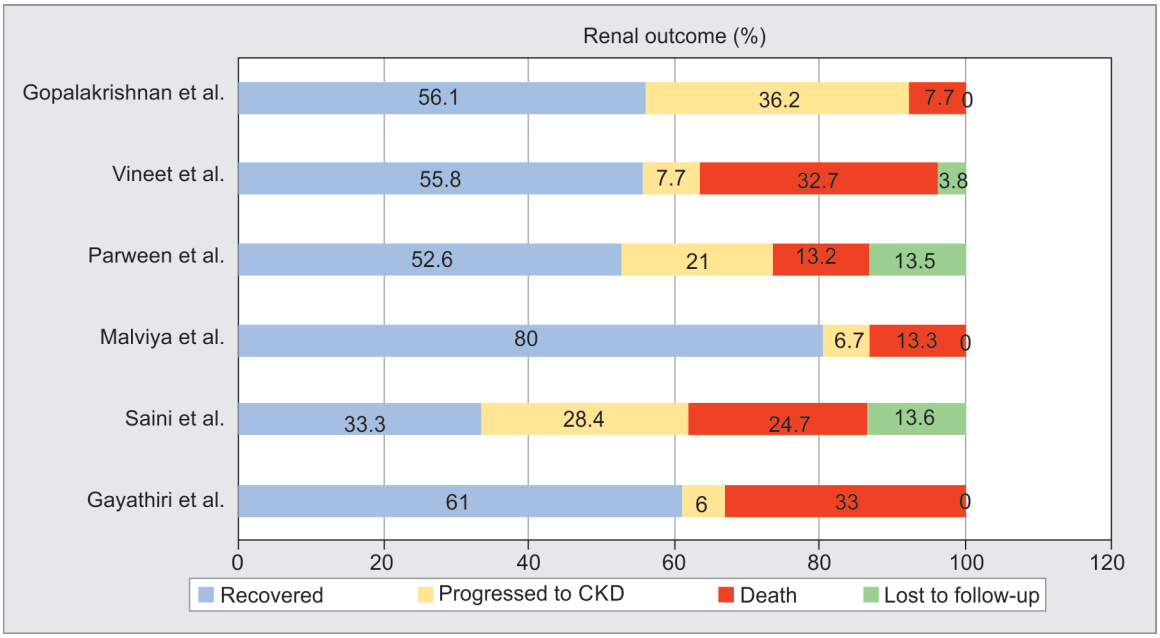


Fig. 1: Renal outcome of PRAKI

persistent anemia, thrombocytopenia with schistocytes in general blood picture and high lactate dehydrogenase levels can help in early diagnosis.

Our study also showed high maternal mortality and morbidity in patients with PRAKI. These findings resonate with Liu et al., who conducted a systematic review and meta-analysis of studies reporting the outcome of AKI in pregnancy.[33] A total of 11 studies were included for analysis, out of which 6 were from China, 2 were from Morocco, and one each from Tunisia, France, and Turkey. Also, PRAKI was associated with a 4.5 times increased risk of maternal death [odds ratio (OR) 4.50, 95% CI 2.73–7.43]. In addition to this, patients with PRAKI had increased morbidity in increased length of intensive care unit (ICU) stay, hemorrhage, HELLP syndrome, and placental abruption. Around 2.4% progressed to an end-stage renal disease requiring dialysis.[33] We could not do meta-analysis because of heterogeneity of defining criteria of PRAKI and outcome measures.

In contrast to our findings, a retrospective cohort study from the United States showed a rising trend of PRAKI over 10 years (2006–2015) due to old age and diabetes, besides other predispositions like ethnicity/race.[34] These findings highlight the variations in the global epidemiology of PRAKI and the importance of generating local data.

Strengths and Implications for Future Research

Our study is the first systematic review analyzing the causes of PRAKI in the Indian subcontinent. The data presented here can guide planners and policymakers for appropriate budget allocation and ending preventable maternal mortality. To guide the reporting of PRAKI in future studies, we have also designed an outline of the case report form shown in Table 5. We hope that structured reporting

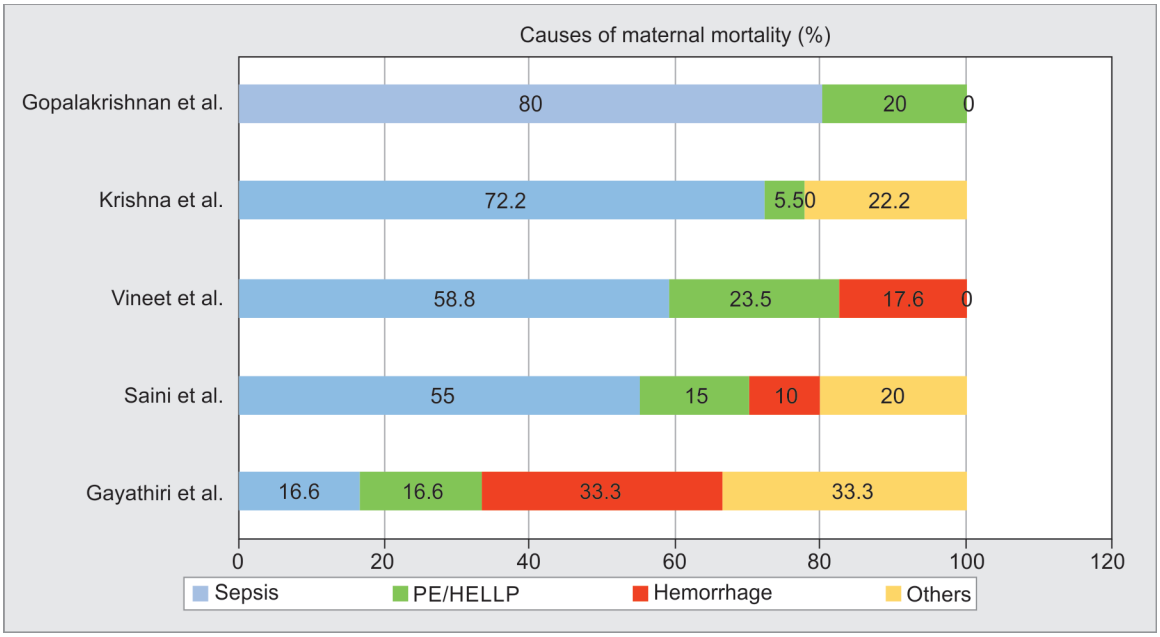


Fig. 2: Causes of maternal mortality in PRAKI

Table 5: Proposal for reporting PRAKI in observational studies

1	Demographic characteristics and obstetric details	Age, gravida, comorbidities, booked/unbooked, ANC visits, mode of delivery (including timing, location, and complications of delivery) Scoring system (SOFA, MEWS) KDIGO stage at admission
2	Incidence/Prevalence of PRAKI	
3	Causes of PRAKI	Sepsis a) Postabortal b) Postnormal vaginal delivery c) Post-LSCS d) Urosepsis e) Other sources (pneumonia, bloodstream, etc.) Hemorrhage a) Antepartum hemorrhage b) Postpartum hemorrhage Pregnancy-induced hypertension and related diseases a) Pre-eclampsia b) Eclampsia c) HELLP d) Acute fatty liver of pregnancy TMAs a) TTP b) HUS c) Atypical HUS Hypovolemia a) Diarrhea b) Hyperemesis gravidarum c) Others Tropical fever a) Malaria b) Dengue c) Leptospirosis d) Scrub typhus e) Others Miscellaneous (drugs, autoimmune, malignancies, chronic liver disease, etc.)

4	Renal outcome at discharge, at 3 months and at 6 months	Complete recovery
		Progressed to chronic kidney disease a) Dialysis independent b) Dialysis dependent
		Lost to follow-up
		Death
5	Obstetric outcome	
6	Fetal outcome	
7	RRT	Indication/modality/total dose/duration
8	Renal biopsy	Indication:
		Findings:
9	Other organs	Patients needing ICU care, mechanical ventilation, vasoactive drugs, blood product transfusion, parenteral nutrition
10	Sepsis (if present)	Source, organisms, sensitivity
11	Temporal evolution of the disease	Renal insult triggering event to AKI interval (in hours)
		Onset of AKI to hospitalization interval (in hours)
		Onset of AKI to hospitalization to dialysis capable facility interval (in hours)

ANC, antenatal case; LSCS, lower segment cesarean section; MEWS, modified early warning score; SOFA, sequential organ failure assessment; TTP, thrombotic thrombocytopenic purpura

across the nation will help guide timely transfer to appropriate healthcare facilities and allocate resources to areas of concern. We emphasize reporting the temporal course of the disease process of PRAKI and its relationship with arrival to dialysis equipped healthcare facility.[35] Reporting the temporal evolution of the disease process will also help guide the triggers for referral to dialysis-equipped centers by the primary and secondary healthcare facilities.

Limitations

A consensus definition of PRAKI is lacking in literature; therefore, the robust data in this field is challenging to synthesize.[36] Our study has the following limitations:

- First, out of the seven studies included for analysis, four were conducted in nephrology departments, and major data from obstetrics would have been missing for various reasons (e.g., patients who recovered with fluid replacement or appropriate antibiotics, patients who did not require intervention by the nephrologist, patients who had AKI related to pre-eclampsia and recovered spontaneously after delivery). Therefore, patients in KDIGO AKI stages 1 and 2 are likely to be missed in this systematic review.
- Second, patients who developed multiple organ failure with AKI and were shifted to ICUs have not been described separately in the studies. This is another subgroup where robust data are missing in the included studies.
- Third, PRAKI is a frequently underdiagnosed problem, as causes like drug-induced renal injury, trauma, anaphylaxis, blood transfusion reactions, and tropical fever have not been discussed in most studies.
- Fourth, there is a lack of any standard definition of PRAKI, and it is unknown whether definitions used for the general population should be applied to pregnant women or not. In our systematic review, there was variability in inclusion criteria and PRAKI definition among different studies, as three studies have used KDIGO definition, three studies have used oliguria and rise in serum creatinine and one study has used need for dialysis as inclusion criteria. This further highlights the urgent need for a standardized reporting system for PRAKI.
- Fifth, several studies reported more than one cause of PRAKI, making it difficult to appropriately classify the patients and assess the disease burden of individual causes. We removed these studies from the systematic review, but it decreased our total sample size.
- Sixth, we could not achieve our secondary objective, which was to estimate the incidence rate of PRAKI among obstetric patients in India. This was because the denominator (i.e., the total number of deliveries in the study period) was not reported in any of the studies. Besides this, as stated above, there was variability in the definition of PRAKI and missing data as studies were mostly from the nephrology department.
- Seventh, the definition of renal recovery has been arbitrarily taken as the return of normal urine output and renal function, but the quantitative definition of renal recovery is lacking in literature as well as in the studies undertaken for this review.

Conclusion

Our study highlights that sepsis is the most important cause of PRAKI in India. PRAKI is associated with significant maternal mortality and morbidity. Indian studies on PRAKI require a standardization of reporting format to generate comparable data.

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